

**REMARKS****A. Status of the Claims**

Prior to the submission of this paper, claims 1-30 were pending. In this paper, however, Applicant has canceled claims 27-30. Accordingly, claims 1-26 are currently pending.

Claims 1-30 have been rejected under 35 U.S.C. § 112, ¶2 as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as his invention.

Claims 1-4 and 6-18 have been rejected under 35 U.S.C. §102(b) as allegedly being anticipated by WO 94/14465 (hereafter “the WO ‘465 application”). Claims 19-30 have been rejected under 35 U.S.C. §102(b) as allegedly being anticipated by JP 63-146829 (“the JP ‘829 patent”).

Claim 5 has been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the WO ‘465 application in view of the JP ‘829 patent.

**B. Claims 1-26 Are Not Indefinite under 35 U.S.C. § 112, ¶2.**

As claims 27-30 have been cancelled herein, Applicant respectfully traverses the rejection of claims 1-26 under 35 U.S.C. §112, ¶2 as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as his invention. The Office Action states that “[i]t is unclear from the specification and the prior art what is meant by ‘accelerated testing’ and how it is different from ‘unaccelerated testing.’” [Office Action, pages 2-3].

Applicant respectfully disagrees and submits that it is within the common general knowledge of the art that “accelerated testing” is used to mean testing in harsh environments for

a short period of time in place of testing under normal storage conditions which takes a long time (i.e., “unaccelerated testing”). For example, testing the stability of a formulation by keeping it at a temperature that is higher than the normal storage temperature for a given period of time would be considered “accelerated testing,” whereas a stability test of the same formulation at the normal storage temperature for a longer period of time would be “unaccelerated testing.” Applicant further submits that those skilled in the art would understand from the specification as well that G-CSF-containing freeze-dried formulations that are allowed to stand at an elevated temperature (e.g., 50 or 60 °C) for a given period of time (e.g., 2 weeks, 1, 2, or 3, months) are being subjected to “accelerated testing.”

Accordingly, Applicant respectfully requests the reconsideration and withdrawal of the rejection of claims 1-26 under 35 U.S.C. § 112, ¶2.

C. Claims 1-4 and 6-18 Are Not Anticipated  
by the WO '465 Application

Applicant respectfully traverses the rejection of claims 1-4 and 6-18 under 35 U.S.C. §102(b) as allegedly being anticipated by the WO '465 Application. Briefly, the WO '465 application fails to teach, disclose, or suggest all of Applicant's claimed elements in the amended claims. Accordingly, the rejection should be withdrawn. MPEP §2131.

Applicant's amended claim 1 recites a stable G-CSF formulation containing a combination of the following three types of amino acids:

- (1) one or more amino acids selected from the group consisting of lysine, histidine, arginine, aspartic acid, glutamic acid, threonine and asparagine;
- (2) one or more amino acids selected from hydrophobic amino acids; and

(3) methionine.

Applicant has reviewed the WO '465 Application and does not see where the WO '465 application teaches, discloses, or suggests a stable G-CSF formulation containing, inter alia, methionine, as recited in Applicant's amended claim 1. Accordingly, because not all claim elements are taught or suggested, the WO '465 application does not anticipate Applicant's amended claim 1. MPEP §2131. For at least similar reasons, Applicant believes that amended claims 2-4 and 6-15, which depend directly or indirectly from claim 1, are not anticipated by the WO '465 application.

With respect to amended claims 16-18, Applicant points out that independent claims 16 and 18 have been amended to recite, inter alia, a formulation having a pH from 5-7 that contains certain combinations of amino acids. More specifically, these combinations are as follows:

**Claim 16**

one or more amino acids selected from the group consisting of lysine, histidine, aspartic acid, glutamic acid, threonine and asparagine; and

one or more amino acids selected from the group consisting of tryptophan and leucine.

**Claim 18**

one or more amino acids selected from the group consisting of lysine, histidine, arginine, aspartic acid, glutamic acid, threonine and asparagine; and

one or more amino acids selected from the group consisting of tryptophan and leucine.

Applicant has reviewed the WO '465 application and does not see where this references teaches, discloses, or suggests formulations at a pH of 5-7 that have the combinations of amino acids recited in Applicant's amended claims 16 and 18. Accordingly, because not all claim elements are taught, the rejection of independent claims 16 and 18 should be withdrawn. MPEP § 2131. Moreover, dependent claim 17 is believed to be patentable for at least similar reasons. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections of claims 16-18 under 35 U.S.C. §102(b).

D. Applicant's Amended Claims 19-26 Are  
Not Anticipated by the JP '829 Patent

As claims 27-30 have been cancelled in this paper, Applicant focuses on claims 19-26 in this section of the response. Applicant respectfully traverses the rejection of claims 19-26 as allegedly being anticipated by the JP '829 Patent.

With respect to claims 19 and 20, Applicant points out that these claims have been amended such that they now depend from claim 18 (in the case of claim 19) or from both 16 or 18 (in the case of claim 20). Applicant has reviewed the JP '829 patent and does not see where the patent teaches, discloses or suggests the combination of amino acids having specified pH values or ranges as recited in claims 19 and 20. Accordingly, because the JP '829 patent fails to teach, disclose, or suggest all of the elements of Applicant's claims 19 and 20, the JP '829 patent does not anticipate claims 19 or 20. MPEP § 2131.

With respect to amended claims 21-26, the JP '829 patent does not appear to teach, disclose, or suggest a formulation containing, inter alia, PTH, as recited in Applicant's claims 21-26. Accordingly, the JP '829 patent does not anticipate amended claims 21-26.

MPEP §2131. Reconsideration and withdrawal of the rejection of these claims is respectfully requested.

E. Applicant's Claim 5 Is Not Obvious  
Over the Cited References

Applicant respectfully traverses the rejection under 35 U.S.C. §103(a) of claim 5 as allegedly being obvious over the combination of the WO '465 application and the JP '829 patent. The traversal is based on at least the following two reasons: (1) there is no motivation to combine the references; and (2) the references teach away from the proposed combination. For at least these reasons, the rejection under 35 U.S.C. §103(a) should be withdrawn. MPEP §2145.

The office action states that the motivation to combine the WO '465 application and the JP '829 patent "is provided by both the references' teachings regarding the benefits of adding phenylalanine, arginine, and methionine, and the appreciation of one skilled in the art that addition of any agent that contributes to stability would have been desirable." [Office Action, page 5]. Applicant, however, does not see any teaching, express or otherwise, about "the benefits of adding phenylalanine, arginine, and methionine" (emphasis added) as alleged by the Office Action. At best, it appears that the WO '465 application discloses a formulation containing phenylalanine and arginine (e.g., Example 11), whereas the JP '829 patent discloses formulations containing arginine and methionine (e.g., page 4 of the English translation). The so-called "benefits" of the combination of all three amino acids are not disclosed in either reference.

Moreover, the WO '465 application teaches away from the combination proposed by the Office Action. On page 9 of the English translation of the WO '465 application, it states that

[i]n a particular embodiment, pharmaceutical preparations are provided that contain amino acids...Possible amino acids include basic amino acids, such as arginine, lysine, ornithine, etc., acidic amino acids, such as glutamic acid, aspartic acid, etc., or aromatic amino acids, such as phenylalanine tyrosine, tryptophane, etc. (emphasis added).

Applicant respectfully submits that methionine is a neutral amino acid (not acidic or basic) and is also not an aromatic amino acid. Accordingly, because the WO '465 application appears to be limited to acidic, basic, or aromatic amino acids, it teaches away from formulations having methionine, a neutral amino acid. Therefore, the rejection of claim 5 under 35 U.S.C. §103(a) should be withdrawn.

**CONCLUSION**

Based on the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims and allowance of this application.

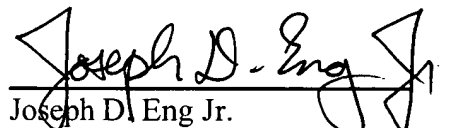
**AUTHORIZATION**

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. 13-4500, Order No. 0263-4051. A DUPLICATE OF THIS DOCUMENT IS ATTACHED.

Respectfully submitted,  
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